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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,725	11/16/2000	Ying Luo	RIGL-008CIP	6653

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BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/715,725	LUO ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *02 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *26,27,29,30 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *26-27, 29-30, 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 25, 2004 and the amendment of November 2, 2004 that appears to be identical to that submitted on May 25, 2004 have been entered. Claims 27 and 30 have been amended and claims 28 and 31 have been canceled. Claims 16-17, 29-30, 32 are currently under prosecution.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant's proper submission of the corrected sequence listing has been entered. It is noted that amendment of the figures to reflect the correction would be appropriate.

4. The following rejections are being maintained:

Claim Rejections - 35 USC 101

5. Claims 26-27, 29-30, 32 remain rejected under 35 USC 112, first paragraph essentially for the reasons previously set forth in the paper mailed February 6, 2004, Section 5 pages 4-7.

Applicant argues that given the identity of SEQ ID NO:8 to SEQ ID NOS:2, 4, 6, one would recognize that SEQ ID NO:8 has p53 modulatory activity and this answers the questions about utility of SEQ ID NO:8,

The argument has been considered but has not been found persuasive because, for the reasons previously set forth, modulation of p53 does not provide specific utility because this activity is clearly shared by many unrelated

polypeptide structure sequences that have different functions. Further, modulation of p53 does not provide substantial activity because it is unknown what association of SEQ ID NO:8 with p53 does (see paragraph bridging pages 6-7 of the previous action). Further, as drawn specifically to claims 27, 30 and 32, it is noted that Applicant is arguing limitations not recited in the claims as currently constituted since the claims are not drawn to modulation of p53, but rather are drawn to increasing transcription from a p53 binding site promoter and additional work would be required to identify the promoter which SEQ ID NO:8 modulates, thus the claims as newly amended do not have substantial utility.

Applicant further argues that submitted Exhibit B, Shiseki et al, Cancer Research, 2003, 2373-2378) supports the Applicants position that a polypeptide having the sequence of SEQ ID NO:8 has p53 modulatory activity and points to the abstract of the paper.

The argument has been considered but has not been found persuasive because contrary to Applicant's argument, the Shiseki et al paper does not support the utility of the claimed invention but rather supports the lack of utility at the time the invention was made. In particular, a review of the Shiseki et al abstract reveals that the authors have identified and characterized p28ING5 wherein it was found that p28ING5 activates the p21/waf1 promoter and induce p21/WAF1 expression and also enhance p43 acetylation and physically interacts with p53, suggesting that p28ING5 may be a significant modulator of p53 function. Although Applicant clearly states in the specification as originally filed that the claimed invention activates p53 binding site controlled promoters, there is no suggestion in the Shiseki et al paper that p28ING5 activates p53 binding site controlled promoters, but rather the authors specifically state that p28ING5 activates the p21/waf1

promoter and that p28ING5 physically associates with p53. Given the comprehensive characterization of p28ING5, it would be surprisingly if its binding to other promoters had not been examined. Thus, it cannot be determined, but appears unlikely, that p28ING5, and by association, that SEQ ID NO:8 in fact activates a p53 binding site controlled promoter. Thus it is clear that additional work must be done in order to determine whether or not SEQ ID NO:8 in fact activates a p53 binding site controlled promoter.

In addition, the reference teaches that there are at least seven ING family proteins and the different biological and biochemical pathways in which these genes are involved are just beginning to be unraveled, but it is clear that they have different functions. A most interesting finding is that their ability to modulate p53 activity, which may depend on their interactions with different HAT and HDAC proteins. Additional analysis, including a genome-wide search for the effect of overexpression of p29ING5 on expression profiles, are necessary to identify which set of genes, including p53-responsive genes, are induced or suppressed by p29ING5. The ING family proteins may also vary in their distribution and regulation of different cell types. (p. 2377, col 2). It is clear that four years after the priority document for the instant application was filed, that function of the SEQ ID NO:8 homologue was unknown. The Shiseki et al reference supports Examiner's finding of lack of utility and the rejection is maintained.

Further, Applicant argues that pursuant to the comments made by Examiner Eyler during the interview of May 3, 2004, that is that post-filing data or reasoned argument would be sufficient to withdrawn the rejection, that the remaining rejections should be withdrawn. The argument has been considered but has not been found persuasive since the reasoned argument is not persuasive for the

reasons set forth above and the post-filing data supports Examiner's finding of lack of utility.

Claim Rejections - 35 USC 112

6. Claim 27 remains rejected under 35 USC 112, first paragraph essentially for the reasons previously set forth in the paper mailed February 6, 2004, Section 4 pages 2-4.

Applicant argues that SEQ ID NO:8 must necessarily have a p-53 modulatory activity identical to that of SEQ ID NO:s 2, 4 and 6 because (a)(1) SEQ ID NOS 2, 4, 6 share a region that is identical in amino acid sequence, each of polypeptides of SEQ ID NOS 2,4, 6 exhibit p53 modulatory activity. Since SEQ ID NO:2 lacks the N-terminal amino acid sequence found in SEQ ID NOS 4 and 6 and SEQ ID NOS 4 and 6 lack a C-terminal amino acid sequence found in SEQ ID NO:2, thus the domain that confers p53-modulatory activity must be that amino acid sequence common to SEQID NOS 2, 4, 6, (b) the polypeptide of SEQ ID NO:8 contains the same amino acid sequence that confers p53-modulatory activity upon the polypeptides of SEQ ID NOS 2,4, 6 and the N-terminal sequence of SEQID NO:8 should not render the polypeptide nonfunctional since this sequence is the same as the N-terminal amino acid sequence of SEQ ID NOS 4 and 6 which have p53 modulatory activity and the C terminal sequence of SEQ ID NO:8 should not render the polypeptide nonfunctional since this is the same as the C-terminal amino acid sequence of the polypeptides of SEQ ID NO:2 which has p53 modulatory activity, (c) apart from its N-terminal 15 amino acids, the polypeptide of SEQ ID NO:8 is identical to the amino acid sequence of known p53 modulatory, p28ING5. Further, Applicant argues that the addition of the limitation

that the claimed SEQ ID NO:8 variant can activate a p53 binding site controlled promoter overcomes the rejection of the claim.

The argument has been considered but has not been found persuasive because it appears that the "p53 modulatory domain" is somewhere within the 200 amino acids of SEQ ID NO:8 from amino acid 30 to 229. Neither the specification nor the art of record provides information drawn to the structure involved with the p53 modulation. Further, neither the specification nor the claims as originally filed are drawn to a "p53 modulatory domain", rather the specification teaches as set forth above that the claimed invention activates p53 binding site controlled promoters. It appears from the submitted Shiseki et al reference that the claimed invention would be expected to bind, not to a p53 binding site controlled promoter, but rather binds to the p21/waf1 binding promoter and that any modulatory activity would be exerted by the expected direct binding of the claimed invention to p53. There is no teaching in the specification of a structure/function relationship for the binding of the claimed invention to p53 within the claimed invention. Thus, the disclosure of the single specific amino acid sequence is insufficient to describe the genus. Finally it is noted that Applicant is arguing limitations not recited in the claim as currently constituted since it is drawn not to p53 modulation, but rather to increased transcription from a p53 binding site controlled promoter. The arguments have been considered but have not been found persuasive and the rejection is maintained.

7. Claims 26-27, 29-30, 32 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2004, Section 6 page 7.

Applicant argues that for the reasons set forth above, one would know how to use the claimed invention. The argument has been considered but has not been found persuasive for the reasons set forth above and the rejection is maintained.

8. Claim 27 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2004, Section 7 pages 7-10.

Applicant argues that the addition of the limitation that the claimed SEQ ID NO:8 variant can activate a p53 binding site controlled promoter in combination with the discussion above overcomes the rejection. The argument has been considered but has not been found persuasive for the reasons set forth previously drawn to the teachings of Zeremski et al, of record, random experimentation and lack of an identified binding site because these apply not only to the IAP binding site but also to the instantly claimed binding site for p53 binding site controlled promoters and as well as for the reasons set forth above. The rejection is maintained.

9. Claim 27 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2004, Section 8 page 10.

Because Applicant did not distinctly and specifically point out the supposed errors in the rejection under 35 USC 112, first paragraph, the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC 112

10. Claims 27, 30, 32 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation drawn to SEQ ID NO:8 or a variant thereof as increasing transcription of a p53 binding site controlled promoter when introduced into a mammalian recited

in claims 27 and 30 has no clear support in the specification and the claims as originally filed. In the amendment after final, Applicant pointed to page 7, lines 8-9 and page 33, lines 5-6 for support for the newly added limitations. The support was considered but was not found persuasive because a review of the cited lines reveals only support for "ING2 activating p53 binding site controlled promoters in the presence or absence of p53". There is nothing drawn to activation leading to increased transcription. The subject matter claimed in claims 27, 30, 32 broadens the scope of the invention as originally disclosed in the specification.

11. Claims 27, 30, 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The claims are drawn to a recombinant ING2 protein, comprising an amino acid sequence having at least 95% sequence identity/having the sequence set forth in SEQ ID NO:8 wherein said recombinant ING2 protein increases transcription from a p53 binding site controlled promoter when introduced into a mammalian cell.

The specification teaches general background information on promoters and teaches that ING2 activates p53 binding site controlled promoters in the presence or absence of p53 on pages 7 and 33 as set forth above.

One cannot extrapolate the teaching of the specification to the enablement of the claims because the Shiseki et al reference calls into question whether or not ING2 in actuality can increase transcription from a p53 binding site controlled promoter. As set forth above, a review of the Shiseki et al abstract reveals that the

authors have identified and characterized p28ING5 wherein it was found that p28ING5 activates the p21/waf1 promoter and induces p21/WAF1 expression and also enhances p43 acetylation and physically interacts with p53, suggesting that p28ING5 may be a significant modulator of p53 function. There is no suggestion in the Shiseki et al paper that p28ING5 activates p53 binding site controlled promoters, but rather the authors specifically state that p28ING5 activates the p21/waf1 promoter and that p28ING5 physically associates with p53. Given the comprehensive characterization of p28ING5, it would be surprisingly if its binding to other promoters had not been examined. Thus, it cannot be determined, but appears unlikely, that p28ING5, and by association, that SEQ ID NO:8 in fact activates a p53 binding site controlled promoter. The specification provides insufficient guidance with regard to these, provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed recombinant ING2 proteins would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

12. All other objections and rejections imposed in the paper mailed February 6, 2004 are hereby withdrawn.

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 872-9306.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
January 14, 2005